UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **March 30, 2022**

REPLIMUNE GROUP, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38596**	**82-2082553**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification Number)

500 Unicorn Park
Woburn, MA 01801
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: **(781) 222-9600**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	REPL	The Nasdaq Stock Market LLC (Nasdaq Global Select Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 8.01 Other Events.

On March 30, 2022, Replimune Group, Inc. (the "Company") issued a news release announcing a data update from its RP1 programs and announcing an update to its plans to expand the development of RP2 and RP3 beyond Phase 1. A copy of the news release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein. The Company undertakes no obligation to update, supplement or amend the materials attached hereto.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	News Release dated March 30, 2022
104	Cover page interactive data file (formatted as Inline XBRL)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REPLIMUNE GROUP, INC.

Date: March 30, 2022

By: /s/ Jean Franchi
Jean Franchi
Chief Financial Officer

Exhibit 99.1

Replimune Provides New Clinical Data, Broad Program Update and Future Development Strategy for its Tumor-Directed Oncolytic Immunotherapies

RP1 combined with Opdivo® (nivolumab) continues to demonstrate deep and durable responses in patients with melanoma and non-melanoma skin cancers (NMSC); new positive initial data in patients with anti-PD1 failed NMSC

Initial data shows clinical activity with RP1 monotherapy in solid organ transplant recipients with cutaneous squamous cell carcinoma (CSCC)

Broad Phase 2 development planned for RP2/RP3 in hard-to-treat tumor types

Virtual investor event to be held today at 8:00 am ET

Woburn, MA, March 30, 2022 – Replimune Group, Inc. (NASDAQ: REPL), a clinical stage biotechnology company pioneering the development of a novel class of tumor-directed oncolytic immunotherapies, today announced updated data from completed cohorts of the Phase 2 part of the IGNYTE clinical trial in non-melanoma skin cancer (NMSC) and melanoma. Additionally, the Company announced new data from the ongoing clinical trial in anti-PD1 failed NMSC and from the ARTACUS clinical trial, a Phase 1b/2 trial of RP1 (vusolimogene oderparepvec) as monotherapy in solid organ transplant recipients with skin cancer. The Company also provided a detailed overview of its RP2/3 Phase 2 development plans. A virtual investor event will be held today at 8:00 a.m. ET to discuss the updated data.

“Today we are pleased to provide a comprehensive clinical update across our pipeline that continues to demonstrate the potential of our oncolytic immunotherapy platform to address a broad range of cancers,” said Philip Astley-Sparke CEO of Replimune. “Updated data from our IGNYTE cohorts in anti-PD1 naïve cutaneous squamous cell carcinoma (CSCC) and anti-PD1 failed melanoma continue to support our two registration-directed studies in these settings. New data presented today also supports our ambition to establish a broad franchise with RP1 in skin cancer, with activity demonstrated in a variety of anti-PD-1/L1 failed non-melanoma skin cancers as well initial data demonstrating utility of RP1 as a monotherapy in solid organ transplant recipient patients where anti-PD1 is contra-indicated. We have seen strong initial data with RP2 monotherapy and in combination with *Opdivo*® which supports the advancement of RP2/3 into new and difficult to treat tumor types. As a result, we are announcing a broad RP2/3 Phase 2 development plan including new clinical trials in advanced/metastatic squamous cell carcinoma of the head and neck (SCCHN), hepatocellular carcinoma (HCC), and colorectal cancer (CRC). We look forward to initiating our clinical trials in these large and underserved markets and delivering meaningful new therapies to patients.”

RP1 in Skin Cancer

The Company is pursuing the development of RP1 for the treatment of multiple skin cancers alone and in combination with anti-PD1 therapy. The Company is today presenting updated data from the Phase 2 part of the IGNYTE clinical trial combined with *Opdivo*.

- **Updated efficacy data for IGNYTE in anti-PD1 naïve NMSC patients treated with RP1 combined with *Opdivo***
  - The Company has completed enrollment of the anti-PD1 naïve NMSC cohort that included patients with CSCC, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), merkel cell carcinoma (MCC), and angiosarcoma (n=32). Ongoing efficacy data is available for 31 patients (1 patient remains on study with no follow assessments as yet).
  - RP1 in combination with *Opdivo* continues to be generally well tolerated, with no new safety signals identified since the last data cut (June 2021).
  - The efficacy data continue to demonstrate that RP1 in combination with *Opdivo* drives deep and durable responses across the range of tumor types enrolled. Further, patients have continued to improve since the last update provided in June 2021.
  - In patients with CSCC, a further complete response (CR) has been documented, and the overall repose rate (ORR) is now 65%, compared to 60% at the June 2021 update. The complete response rate remains unchanged at 47% (i.e. including the additional patients enrolled). Updated response rates in BCC, MCC and angiosarcoma were 25%, 75% and 67% respectively with multiple complete responses documented, indicating potential utility beyond CSCC.
  - The Company believes these data strongly suggests differentiation versus anti-PD1 therapy alone and provides strong validation of the current registration-directed CERPASS clinical trial in CSCC, with the primary data readout expected in early 2023.

- **Updated efficacy data for IGNYTE in both anti-PD1 failed and anti-PD1 naïve melanoma patients treated with RP1 combined with *Opdivo***
  - Thirty-six patients were enrolled as previously reported in melanoma (which included anti-PD1 naïve and failed cutaneous melanoma, mucosal and uveal melanoma).
  - The data shows that RP1 combined with *Opdivo* continues to demonstrate deep and durable responses in patients with melanoma, which tend to deepen over time.
  - ORR in anti-PD1 naïve cutaneous melanoma remains at 62.5%.
  - Sixteen patients had cutaneous melanoma and had previously failed checkpoint therapy, with a current ORR of 37.5% (an improvement from the 31% ORR reported in the June 2021 update), including two complete responses.
  - Based on the previously reported initial data, the Company initiated a registration-directed 125 patient cohort of anti-PD1 failed cutaneous melanoma where an initial interim readout is expected in late 2022.

- **New efficacy data for IGNYTE in anti-PD(L)-1 failed NMSC patients treated with RP1 combined with *Opdivo***
  - The Company is actively enrolling a 30-patient cohort of RP1 in combination with *Opdivo* in anti-PD(L)-1 failed NMSC patients.
  - As of the cutoff date for this initial data cut (n=12), the ORR in this group was 33.3% with responses having been observed in anti-PD(L)-1 failed CSCC, MCC and angiosarcoma, including one complete response. Other patients who remain on study with a shorter follow up are also showing tumor shrinkage.
  - The Company believes the clear activity of RP1 combined with *Opdivo* in anti-PD(L)-1 failed patients represents a new potential therapeutic option for these patients and supports the broad potential for RP1 in skin cancers, including those with anti-PD(L)-1 failed disease.

- **New safety and efficacy data from the Phase 1b/2 ARTACUS trial evaluating RP1 monotherapy in solid organ transplant recipients with CSCC**
    - The ARTACUS trial is a 65-patient clinical trial with potential registrational intent, assessing the safety and efficacy of RP1 monotherapy in solid organ transplant recipients with skin cancer.
    - While numbers are small, RP1 monotherapy in solid organ transplant patients, which represents a significantly immune suppressed population, has so far demonstrated a similar safety profile to that observed in patients who are not immune suppressed.
    - Initial clinical evidence of activity has been seen, with two of six patients (33%) achieving response, with one complete response and one partial response.

"The frequency, depth and durability of responses seen across a range of skin cancers with RP1 alone and combined with *Opdivo*, including in anti-PD1 failed disease, suggests broad utility of the approach," said Professor Kevin Harrington of The Institute of Cancer Research, London and The Royal Marsden NHS Foundation Trust, who will today present the new RP1 data. "Based on this data, I look forward to seeing the results of the registration-directed studies in CSCC and anti-PD1 failed melanoma and the potential provision of a new treatment paradigm for these patients."

RP2/3 Development Strategy

RP2 leverages the Company's platform to express an anti-CTLA-4 antibody, in addition to the GALV-GP R- and GM-CSF expressed by RP1. The Company will review data from the Phase 1 clinical trial of RP2 alone and in combination with *Opdivo* and announce its development strategy for the Phase 2 clinical development of RP2/3. After fully enrolling patients in the RP2 monotherapy (n=9) and combination with *Opdivo* (n=30) cohorts in the Phase 1 clinical trial with RP2 (data presented in Nov 2020 and Nov 2021), a further cohort of Phase 1 patients with tumor types of particular interest (gastro-intestinal [GI] cancers, breast cancer, lung cancer, head and neck cancer and uveal melanoma) was recently opened, with the first patients having been enrolled and from which initial data is expected later in the year.

RP3 further expresses CD40L and 4-1BBL in addition to anti-CTLA-4 and GALV-GP R-, is intended to induce a broad and potent anti-tumor immune response, and for which a Phase 1 clinical trial is also underway. As monotherapy the Company has dosed three patients at a low dose and three at a high dose in a variety of hard-to-treat salvage therapy patients with injections of RP3 into both superficial and deep tumors, including injections into the lung and liver. The higher dose level has been confirmed as the recommended Phase 2 dose (RP2D). A seventh patient has also recently been enrolled such that three HSV seronegative patients in total have been treated at the RP2D. The first six patients enrolled in this Phase 1 clinical trial had heavily pre-treated advanced sarcoma, esophageal cancer, colorectal cancer, head and neck cancer and melanoma. Three of the six patients (with melanoma and colorectal cancer) died due to disease progression approximately two to four months from initiating the study, indicating the advanced nature of disease of the patients enrolled. Two other patients also had rapid progressive disease, and one patient with esophageal cancer had stable disease out to one year. Thus, while no new safety signals having been observed as compared to RP1 or RP2, based on the patients enrolled it is too early to draw any conclusions as to efficacy. Enrollment into the cohort of patients dosed with RP3 combined with *Opdivo* has also recently commenced. This cohort will focus on enrolling patients with GI cancers, breast cancer, lung cancer and head and neck cancer. Initial data for the combination cohort is expected towards the end of the year. Additional patients will also be dosed as monotherapy.

RP2/3 Phase 2 Clinical Development Plan

The Phase 2 development plan for RP2 and RP3 is intended to target tumor types in large underserved markets, including where liver metastases are common, as well as patients with primary liver cancer, and patients with early disease where the objective of treatment would be to achieve cure. This includes the development of RP2/3 in combination with the current standard of care (SOC), including immunotherapy, chemotherapy and radiation, and in settings following the current SOC.

The following indications for signal finding single arm Phase 2 clinical trials have been identified which meet these criteria:

- Locally advanced (LA) and 1L recurrent SCCHN in combination with chemoradiation followed by anti-PD1 therapy, or SOC chemotherapy and anti-PD1 therapy, respectively. The Company's objective is to also initiate a randomized controlled registration directed program in LA SCCHN in parallel with single arm signal finding development.
- 1L and 2L hepatocellular carcinoma (HCC) in combination with SOC immunotherapy and anti-PD1 therapy respectively.
- 3L micro-satellite stable colorectal cancer (CRC) in combination with anti-PD1 therapy.
- Additional signal finding work is also intended in other indications.

Replimune has a clinical trial collaboration and supply agreement with BMS for the supply of *Opdivo* in its clinical trial program with RP2/3.

The RP2/3 phase 2 program is expected to initiate around the year end.

The Company believes that development in this combination of clinical indications provides a risk balanced approach to delivering substantial value across a range of underserved tumor types with early to later stage disease, each with clear unmet need, and in combination with a range of other anti-cancer approaches where clinical synergy may reasonably be expected to be seen. The decision as to whether RP2 or RP3 will be used in these clinical trials will be made later in the year, following generation and analysis of further clinical data with RP2 and RP3 in their respective ongoing Phase 1 clinical trials.

"RP2 and RP3 represent an exciting new potential approach to treating a range of difficult to treat tumor types, including head and neck cancer, gastro-intestinal cancer and HCC patients who are underserved by current treatment approaches," said Dr. Muneeb Ahmed, Chief of Vascular and Interventional Radiology at Beth Israel Deaconess Medical Center and Associate Professor at Harvard Medical School. "I look forward to participating in the planned Phase 2 program as we explore the breadth of clinical activity with RP2/3 across a range of early to later stage disease settings."

The data from this clinical update and an overview of the rationale and the RP2/3 development strategy can be found in the presentation for today's investor event, linked here.

Opdivo® is a trademark of Bristol-Myers Squibb Company.

Investor event and webcast information

Replimune will host a virtual investor event today, Wednesday, March 30, 2022 at 8:00 a.m. ET. The webcast and slides will be accessible live under "Events & Presentations" on the Investors page of the Company's website at www.replimune.com or by clicking here. A replay of the event will be available on Replimune's website.

About CERPASS

CERPASS is Replimune's registration-directed randomized, global Phase 2 clinical study to compare the effects of Libtayo® alone versus a combination of Libtayo and Replimune's investigational oncolytic immunotherapy RP1. The clinical trial is enrolling 180 patients with locally advanced or metastatic cutaneous squamous cell carcinoma (CSCC) who are naïve to anti-PD1 therapy. The clinical trial will evaluate complete response (CR) rate and overall response rate (ORR) as its two primary efficacy endpoints as assessed by independent review, as well as duration of response, progression-free survival (PFS), and overall survival (OS) as secondary endpoints. The study is being conducted under a clinical trial collaboration agreement with Regeneron in which the costs of the trial are shared and full commercial rights retained by Replimune. Libtayo is being jointly developed by Regeneron and Sanofi. Libtayo® is a registered trademark of Regeneron.

About IGNYTE

IGNYTE is Replimune's multi-cohort Phase 1/2 trial of RP1 plus *Opdivo*®. There are 4 tumor specific cohorts currently enrolling in this clinical trial including a 125-patient cohort in anti-PD1 failed cutaneous melanoma. This cohort was initiated after completing enrollment in a prior Phase 2 cohort in the same clinical trial of approximately 30 patients with melanoma. The additional cohorts are in non-melanoma skin cancers which includes both naïve and anti-PD1 failed CSCC, in anti-PD1 failed microsatellite instability high, or MSI-H/dMMR tumors and anti-PD(L)-1 failed non-small cell lung cancer (NSCLC). This trial is being conducted under a collaboration and supply agreement with Bristol-Myers Squibb Company. *Opdivo*® is a trademark of Bristol-Myers Squibb Company.

About RP1

RP1 is Replimune's lead product candidate and is based on a proprietary new strain of herpes simplex virus engineered and genetically armed to maximize tumor killing potency, the immunogenicity of tumor cell death, and the activation of a systemic anti-tumor immune response.

About RP2 & RP3

RP2 and RP3 are derivatives of RP1 that express additional immune-activating proteins. RP2 expresses an anti-CTLA-4 antibody-like molecule and RP3 additionally expresses the immune co-stimulatory pathway activating proteins CD40L and 4-1BBL. RP2 and RP3 are intended to provide targeted and potent delivery of these proteins to the sites of immune response initiation in the tumor and draining lymph nodes, with the goal of focusing systemic immune-based efficacy on tumors and limiting off-target toxicity.

About Replimune

Replimune Group, Inc., headquartered in Woburn, MA, was founded in 2015 with the mission to transform cancer treatment by pioneering the development of novel tumor-directed oncolytic immunotherapies. Replimune's proprietary RPx platform is based on a potent HSV-1 backbone with payloads added to maximize immunogenic cell death and the induction of a systemic anti-tumor immune response. The RPx platform has a unique dual local and systemic mechanism of action (MOA) consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor derived antigens and altering of the tumor microenvironment (TME) to ignite a strong and durable systemic response. This MOA is expected to be synergistic with most established and experimental cancer treatment modalities, and, with an attractive safety profile the RPx platform has the versatility to be developed alone or combined with a variety of other treatment options. For more information, please visit www.replimune.com.

Forward Looking Statements

This press release contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about the design and advancement of our clinical trials, the timing and sufficiency of our clinical trial outcomes to support potential approval of any of our product candidates, our goals to develop and commercialize our product candidates, patient enrollments in our existing and planned clinical trials and the timing thereof, our upcoming investor event, and other statements identified by words such as “could,” “expects,” “intends,” “may,” “plans,” “potential,” “should,” “will,” “would,” or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs and timing of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, political and global macro factors including the impact of the coronavirus as a global pandemic and related public health issues, the escalating Russian-Ukrainian conflict and related global economic environment, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other reports we file with the Securities and Exchange Commission. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

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